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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/065,330	04/23/98	WALKER A	2500.097US2

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EXAMINER	
SAOUD, C	

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 12/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

PTO-90C (Rev. 2/95)

Office Action Summary	Application No. 09/065,330	Applicant(s) WALKER
	Examiner Christine Saoud	Group Art Unit 1647

☒ Responsive to communication(s) filed on *Sep 18, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-6, 9-11, and 14-16* is/are pending in the application.

Of the above, claim(s) *14-16* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6 and 9-11* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claim 9 has been amended, claim 12 has been canceled, and claims 14-16 have been added as requested in the amendment of paper #15, filed 18 September 2000. Claims 1-6 and 9-11 and 14-16 are pending in the instant application.

2. Newly submitted claims 14-16 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are directed to a method of using the polypeptide. The invention of these claims is related to the elected invention as are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of the original election could be used in an entirely different manner, such as in a method of producing antibodies rather than in a method of treating cancer.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 14-16 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

3. Claims 1-6 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Cooke et al. (U.S. Pat. No. 4,725,549) and A. M. Walker (TEM, 5(5): 195-200) in view of Maciejewski et al. (J. Biol. Chem. 270(17): 27661-27665, 1995, for the reasons of record in paper #13.

Applicant argues that Walker and Maciejewski et al. teach away from each other. This argument is not persuasive because Maciejewski et al. teach that a mutation of serine to glutamic acid mimics phosphorylation and Walker teaches that phosphorylation results in antagonistic activity. Applicant argues that the specification teaches that the "serine 90 phosphorylated bovine prolactin was reported to be biologically inactive". However, this result only demonstrates that this form of prolactin did not stimulate cell proliferation in the Nb2 rat lymphoma bioassay, and says nothing to whether the prolactin was an antagonist or not. Therefore, Maciejewski et al. does not teach away from Walker. Antagonistic activity does not require inhibition of cell proliferation, but rather, antagonism of the native ligand and native biological activity of the native ligand. Therefore, a lack of cell proliferation could also be considered antagonism because it counteracts or neutralizes native prolactin (i.e. lack of cell proliferation), absent evidence to the contrary.

Applicant argues that Maciejewski et al. suggest that phosphorylated prolactin is not an antagonist. This argument is not persuasive because Maciejewski et al. was not cited for its teaching of whether the compound was an antagonist, but rather for the teaching that substitution of serine with glutamic or aspartic acid mimic phosphorylation. Maciejewski et al. is essentially

silent to the biological activity of antagonism and does not appear to teach away, contrary to Applicant's assertion. This is especially in light of Walker which recites at page 197 that "phosphorylated PRL clearly acts as a superantagonist, with approximately one-tenth the concentration of phosphorylated Prl neutralizing the growth-promoting effects of the rest of the PRL" and "[w]hether this superantagonism is achieved by a much increased affinity for the receptor or initiation of a different signal cascade within the cell is unknown at present". Therefore, Walker teaches that binding to the receptor is not required for antagonism, contrary to Applicant's assertions.

Applicant argues that the examiner has not provided motivation for the combination of references. This argument is not persuasive because such motivation was provided in the previous Office action. One of ordinary skill in the art would be motivated to substitute another amino acid which would mimic phosphorylation for this serine because Walker teaches that this serine is important for biological activity and phosphorylation creates an antagonist of prolactin. I

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant argues that Maciejewski et al. do not teach that substituted prolactin acts as a prolactin receptor antagonist. Applicant is correct; the Examiner misstated the reference. However, Maciejewski et al. do teach that substitution of the prolactin mimics phosphorylation and Walker teaches that phosphorylation results in a superantagonist, be it an antagonist of receptor binding or by antagonism of the biological activity via another mechanism (see Walker at page 197).

Applicant again argues that Maciejewski et al. suggest that phosphorylated prolactins could not be used as antagonist because of the disclosure that they are unable to bind or activate prolactin receptors. This argument is unsupported by any facts of record. The disclosure that the phosphorylated protein does not bind the receptor does not mean that the protein is not an antagonist. The Examiner mistakenly referred to "prolactin receptor antagonist". This was a poor choice of words, in light of the teachings of Walker and also due to the number of different ways a compound could antagonize the biological effects of another compound. However, it still does not mean that a *prima facie* case of obviousness was not presented in the previous Office action.

Applicant continues to argue that Maciejewski et al. do not teach that mutation of serine creates an antagonist. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Maciejewski et al. was not cited for it's teaching of antagonistic activity, but rather that substitution of serine with

glutamic or aspartic acid mimics phosphorylation. Walker teach that phosphorylation results in antagonism. Therefore, one would expect the substitution of serine with glutamic or aspartic acid to mimic phosphorylation and to result in antagonism, absent evidence to the contrary.

Applicant argues at page 7 that there is no suggestion or motivation to modify prolactin because it would make the protein inactive. This argument is not persuasive because the inability of the mutated prolactin to stimulate cell proliferation does not mean that it is useless or undesirable. Rather, the fact that it does not stimulate cell proliferation would support the findings of Walker, which identify the phosphorylated protein as an antagonist, thereby leading one to conclude that the substitution which mimics phosphorylation would also lead to antagonism, as taught by Walker. Again, Applicant states that because Maciejewski et al. do not teach the use of phosphorylated prolactins as antagonists. Applicant is correct, but the cited reference of Walker was relied upon for this teaching.

Applicant argues that the disadvantage of dephosphorylation was not taught in the cited reference, but rather in the instant specification. This argument is not persuasive because Maciejewski et al. do mention the advantage of mutation of serine to create mimics of phosphorylation due to the variability in phosphorylation of the native protein. One does not need the teachings of the instant specification to realize the advantage of mimicking phosphorylation by mutation to another amino acid in that one of ordinary skill in the art would readily recognize the advantage of such since it was already taught in the art as evidenced by Maciejewski et al.

Therefore, the invention as claimed would have been prima facie obvious over the prior art of record for the reasons of record and for the reasons provided above.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

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Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 4, 2000

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud